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L18 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:874778 HCAPLUS
DOCUMENT NUMBER: 139:347730
TITLE: Auto-stimulating cells and methods for making and using the same
INVENTOR(S): Tykocinski, Mark L.; Zheng, Guoxing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S. Ser. No. 957,056.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003206917	A1	20031106	US 2002-205524	20020725
US 6316256	B1	20011113	US 2000-476828	20000103
US 2002037583	A1	20020328	US 2001-957056	20010920
WO 2004011673	A1	20040205	WO 2003-US23039	20030723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004161806	A1	20040819	US 2004-775942	20040210
PRIORITY APPLN. INFO.:			US 2000-476828	A3 20000103
			US 2001-957056	A2 20010920
			US 2002-398050P	P 20020722
			US 2002-205524	A 20020725

AB Methods for transferring one or more proteins to a cell are disclosed. The protein or proteins to be transferred are in the form of a fusion protein, and contain at least one domain encoding for a protein or peptide having trans signaling and/or adhesion function. The fusion protein is transferred to a cell by binding to a lipidated protein, which has been incorporated into the cell membrane. In an addnl. aspect of the invention, methods of making fusion proteins having cis signaling capabilities, as well as the ability to bind with receptors on the cell's own surface, are provided. Fusion proteins incorporating GPI or a homing element, and a costimulator or inhibitor domain can also be directly transferred to the cell surface. Methods for using cells which have undergone **protein transfer** according to the present methods are also disclosed. This includes use in a cancer vaccine, use for treatment of cancer or autoimmune disease, and use in determining costimulator threshold levels. Recombinant fusion protein containing B7-1 extracellular domain linked to Fcγ1 was transferred to cells precoated with palmitated protein A.

IC ICM A61K039-00
ICS C12N005-08
NCL 424185100; 435372000
CC 9-2 (Biochemical Methods)

Section cross-reference(s): 1, 15

- ST auto stimulating cell fusion **protein transfer**;
chimeric B7 1 IgG1 Fc fragment **protein transfer**;
palmitated protein A transfer costimulating chimeric Ig fragment
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(4-1BB ligand, costimulator domain of, in fusion protein;
auto-stimulating cells, their preparation by transferring fusion proteins
having trans signaling or adhesion function, and their use in therapy
and assays)
- IT Proteins
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
BIOL (Biological study); PREP (Preparation)
(A, palmitated; auto-stimulating cells, their preparation by transferring
fusion proteins having trans signaling or adhesion function, and their
use in therapy and assays)
- IT Cell activation
(B cell, by fusion protein; auto-stimulating cells, their preparation by
transferring fusion proteins having trans signaling or adhesion
function, and their use in therapy and assays)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B7 h, costimulator domain of, in fusion protein; auto-stimulating
cells, their preparation by transferring fusion proteins having trans
signaling or adhesion function, and their use in therapy and assays)
- IT Interleukin 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B7-1-Fcyl fusion protein effect on T cell production of;
auto-stimulating cells, their preparation by transferring fusion proteins
having trans signaling or adhesion function, and their use in therapy
and assays)
- IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD24, costimulator domain of, in fusion protein; auto-stimulating
cells, their preparation by transferring fusion proteins having trans
signaling or adhesion function, and their use in therapy and assays)
- IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD30 ligand, costimulator domain of, in fusion protein;
auto-stimulating cells, their preparation by transferring fusion proteins
having trans signaling or adhesion function, and their use in therapy
and assays)
- IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD40-L (antigen CD40 ligand), costimulator domain of, in fusion
protein; auto-stimulating cells, their preparation by transferring fusion
proteins having trans signaling or adhesion function, and their use in
therapy and assays)
- IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD48, costimulator domain of, in fusion protein; auto-stimulating
cells, their preparation by transferring fusion proteins having trans
signaling or adhesion function, and their use in therapy and assays)
- IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD70, costimulator domain of, in fusion protein; auto-stimulating
cells, their preparation by transferring fusion proteins having trans
signaling or adhesion function, and their use in therapy and assays)
- IT Animal cell line
(Daudi; auto-stimulating cells, their preparation by transferring fusion

- proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Animal cell line
(EL4; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Hemopoietins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(FLT3 ligand, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICAM-1 (intercellular adhesion mol. 1), costimulator domain of, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICAM-2 (intercellular adhesion mol. 2), costimulator domain of, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICAM-3 (intercellular adhesion mol. 3), costimulator domain of, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(IgG1, fusion products, with B7-1; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Animal cell line
(JY; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Animal cell line
(K562; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LIGHT, costimulator domain of, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), with peptide antigen, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(OX-40, ligand, costimulator domain of, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)

- IT Cell migration
(T cell infiltration, tumor-infiltrating, **protein transfer** to; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TNFSF7 (tumor necrosis factor superfamily member 7), costimulator domain of, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TRAIL (tumor necrosis factor-related apoptosis-inducing ligand), as inhibitor domain in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT B cell (lymphocyte)
Mast cell
Neutrophil
(activation, by fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as homing element in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Fas ligand
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as inhibitor domain in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Animal tissue culture
Cell
Drug delivery systems
Human
Therapy
Transplant and Transplantation
(auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT CD4 (antigen)
CD8 (antigen)
Fusion proteins (chimeric proteins)
Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Analysis
(biochem., in determining costimulator threshold levels; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Ligands
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cDNA encoding membrane receptor binding to cell surface; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)

- IT Autoimmune disease
Neoplasm
(cells for use in treatment of; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Immunostimulation
(cellular; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT CD80 (antigen)
CD86 (antigen)
LFA-3 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(costimulator domain of, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Immunity
(disorder, alloimmune disease; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Blood vessel
(endothelium, **protein transfer** to cell of; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Gene, animal
cDNA
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(for membrane protein binding receptor on cell surface; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fragments, Fc, chimeric, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antigen-presenting cell
(fusion protein activating; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Apoptosis
(fusion protein having domain inducing, in T cell; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Adhesion, biological
(fusion protein with motif for; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fusion proteins binding to cell surface; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heat-stable, costimulator domain of, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)

- and assays)
- IT Glycophospholipids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Homing receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in fusion proteins; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT T cell (lymphocyte)
(infiltration, tumor-infiltrating, **protein transfer** to; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Protein motifs
(inhibitor domain, in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Skin
(keratinocyte, **protein transfer** to; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Lymphocyte
(killer cell, activation, by fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT T cell (lymphocyte)
(killer cell, **protein transfer** to lymphokine-activated; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cell activation
(killer lymphocyte, by fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cell membrane
(lipidated protein in, for fusion **protein transferral** to cell; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipidated, fusion **protein transferral** to cell by binding to; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cell activation
(mast cell, by fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(membrane, binding receptor on cell surface, cDNA encoding; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)

- IT T cell (lymphocyte)
 - (natural killer, **protein transfer** to;
auto-stimulating cells, their preparation by transferring fusion proteins
having trans signaling or adhesion function, and their use in therapy
and assays)
- IT Cell activation
 - (neutrophil, by fusion protein; auto-stimulating cells, their preparation by
transferring fusion proteins having trans signaling or adhesion
function, and their use in therapy and assays)
- IT Cell proliferation
 - (of T cells painted with chimeric conjugate; auto-stimulating cells,
their preparation by transferring fusion proteins having trans signaling or
adhesion function, and their use in therapy and assays)
- IT Glycophospholipids
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphatidylinositol-containing, in fusion proteins; auto-stimulating
cells, their preparation by transferring fusion proteins having trans
signaling or adhesion function, and their use in therapy and assays)
- IT Virus
 - (**protein transfer** to T cell having specificity for
peptide antigen of; auto-stimulating cells, their preparation by
transferring fusion proteins having trans signaling or adhesion
function, and their use in therapy and assays)
- IT Peptides, biological studies
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**protein transfer** to T cell having specificity for
viral antigenic; auto-stimulating cells, their preparation by transferring
fusion proteins having trans signaling or adhesion function, and their
use in therapy and assays)
- IT Muscle
 - Nerve
 - Pancreatic islet of Langerhans
 - (**protein transfer** to cell of; auto-stimulating
cells, their preparation by transferring fusion proteins having trans
signaling or adhesion function, and their use in therapy and assays)
- IT Lymphokines
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**protein transfer** to killer cell activated by;
auto-stimulating cells, their preparation by transferring fusion proteins
having trans signaling or adhesion function, and their use in therapy
and assays)
- IT Embryo, animal
 - Mesenchyme
 - (**protein transfer** to stem cell of; auto-stimulating
cells, their preparation by transferring fusion proteins having trans
signaling or adhesion function, and their use in therapy and assays)
- IT B cell (lymphocyte)
 - Basophil
 - CD4-positive T cell
 - CD8-positive T cell
 - Chondrocyte
 - Dendritic cell
 - Eosinophil
 - Fibroblast
 - Hematopoietic precursor cell
 - Mast cell
 - Monocyte
 - Neutrophil
 - Osteoblast
 - Stem cell

- T cell (lymphocyte)
(**protein transfer** to; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Cell activation
(second domain of fusion protein having costimulator domain for; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(single chain, scFv, as homing element in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Signal transduction, biological
(trans or cis signaling, fusion protein with motif for; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Protein motifs
(trans signaling or adhesion; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-associated, **protein transfer** to T cell having specificity for; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Vaccines
(tumor; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Antitumor agents
(vaccines; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Infection
(viral, treatment of; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ , B7-1-Fc γ 1 fusion protein effect on T cell production of; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT 57-10-3D, Palmitic acid, reaction products with protein A 264888-18-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT 62031-54-3, FGF 83869-56-1, GM-CSF 127464-60-2, Vascular endothelial growth factor 207621-35-0, TRANCE
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in fusion protein; auto-stimulating cells, their preparation by transferring fusion proteins having trans signaling or adhesion function, and their use in therapy and assays)
- IT 14464-31-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with protein A; auto-stimulating cells, their preparation by
transferring fusion proteins having trans signaling or adhesion
function, and their use in therapy and assays)

IT 26062-48-6, Polyhistidine

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)

(tag in fusion protein; auto-stimulating cells, their preparation by
transferring fusion proteins having trans signaling or adhesion
function, and their use in therapy and assays)

L18 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:698243 HCAPLUS

DOCUMENT NUMBER: 139:349391

TITLE: New design for cancer vaccine and artificial veto
cells: An emerging palette of protein paints

AUTHOR(S): Tykocinski, Mark L.; Chen, Aoshuang
; Huang, Jui-Han; Weber, Matthew C.; Zheng,
Guoxing

CORPORATE SOURCE: Department of Pathology and Laboratory Medicine,
University of Pennsylvania, Philadelphia, PA, USA

SOURCE: Immunologic Research (2003), 27(2-3), 565-574

CODEN: IMRSEB; ISSN: 0257-277X

PUBLISHER: Humana Press Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Antigen-presenting cells (APC) can be refaced with "protein
paints" that change the appearance of their T cell-oriented trans signal
arrays. Our group has developed three categories of protein paints
suitable for this kind of APC engineering: artificial
glycosylphosphatidylinositol (GPI) proteins, palmitated-protein
A:Fcγ fusion protein conjugates, and trans signal converter
proteins. Protein paints have been devised with either immune enhancement
or suppression in mind. Costimulator · GPI and palmitated-protein
A:costimulator · Fcγ conjugates can be used to augment the
immune-activating potential of tumor cells. Alternatively, protein paints
can be designed to transform APC into artificial veto cells, in essence
creating Trojan horses capable of inhibiting pathogenic T cells. Trans
signal converter proteins (TSCP) have been devised for this purpose. Our
first paradigmatic inhibitory TSCP, CTLA-4 · Fas ligand, binds to
APC, and in so doing, simultaneously blocks B7 costimulation (via CTLA-4)
and sends inhibitory trans signals (via Fas ligand) to T cells with
dramatic efficacy. **Protein transfer** offers a number of
advantages over gene transfer in facilitating quant. and combinatorial
protein expression and simplifying in vivo applications; the palette of
protein paints with immunotherapeutic potential will undoubtedly continue
to evolve.

CC 15-0 (Immunochemistry)

ST review **protein transfer** costimulation cancer vaccine
veto cell

IT Antigen-presenting cell

Immunostimulation

Immunotherapy

Protein engineering

Signal transduction, biological

T cell (lymphocyte)

(**protein transfer** of immunostimulatory mols. for
cancer vaccine and artificial veto cells to modify APC-to-T cell trans
signals)

IT Proteins

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**protein transfer** of immunostimulatory mols. for
cancer vaccine and artificial veto cells to modify APC-to-T cell trans
signals)

IT Lymphocyte
(suppressor cell, veto cell; **protein transfer** of
immunostimulatory mols. for cancer vaccine and artificial veto cells to
modify APC-to-T cell trans signals)

IT Vaccines
(tumor; **protein transfer** of immunostimulatory mols.
for cancer vaccine and artificial veto cells to modify APC-to-T cell
trans signals)

IT Antitumor agents
(vaccines; **protein transfer** of immunostimulatory
mols. for cancer vaccine and artificial veto cells to modify APC-to-T
cell trans signals)

REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:363910 HCAPLUS

DOCUMENT NUMBER: 139:132140

TITLE: Quantitative interplay between activating and
pro-apoptotic signals dictates T cell responses

AUTHOR(S): **Chen, Aoshuang; Zheng, Guoxing;**
Tykocinski, Mark L.

CORPORATE SOURCE: Department of Pathology and Laboratory Medicine,
University of Pennsylvania, Philadelphia, PA,
19104-4283, USA

SOURCE: Cellular Immunology (2003), 221(2), 128-137
CODEN: CLIMB8; ISSN: 0008-8749

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antigen-presenting cells (APC) can express surface ligands with both T
cell activating and inhibitory capacities, prompting the question of how
responding T cells integrate opposing trans signals concurrently delivered
by APC. To address this question in a quant. fashion, the authors turned
to **protein transfer** as a unique exptl. approach that
is well-suited for addressing such questions from a quant. standpoint.
Costimulatory (either B7-1•Fcγ1 or Fcγ1•4-1BBL) and
pro-apoptotic (Fcγ1•FasL) Fc fusion proteins were quant.
"painted" in varying ratios onto surrogate APC pre-coated with
palmitated-protein A, the latter serving as a surface anchor. Evaluating
the signaling potential of these various painted cells in a standard in vitro
T cell proliferation assay, the authors demonstrated that at a given level
of TCR triggering, the quant. balance between costimulator (B7-1 or
4-1BBL) and FasL dictates the magnitude of the proliferative T cell
response. Furthermore, when the costimulator d. is kept constant, there is
also a quant. balance between TCR-directed and FasL signals. Interesting
species-specific naive vs. memory T cell subset differences emerged with
regard to susceptibility to Fas-mediated apoptosis and costimulator:FasL
opposition. Taken together, these data demonstrate for the first time a
quant. interplay between activating and pro-apoptotic trans signals that
dictates the magnitude of T cell responses.

CC 15-2 (Immunochemistry)

ST apoptosis costimulatory mol signal T cell activation

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(CD137L; T-cell response to interplay between costimulatory and pro-apoptotic signaling ligands)

IT TCR (T cell receptors)
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (CD3 complex; T-cell response to interplay between costimulatory and pro-apoptotic signaling ligands for activation via)

IT Cell activation
 Cell proliferation
 (T cell; in response to interplay between costimulatory and pro-apoptotic signaling ligands)

IT Apoptosis
 Signal transduction, biological
 (T-cell response to interplay between costimulatory and pro-apoptotic signaling ligands)

IT CD80 (antigen)
 Fas ligand
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (T-cell response to interplay between costimulatory and pro-apoptotic signaling ligands)

IT Antigen-presenting cell
 (T-cell response to interplay between costimulatory and pro-apoptotic signaling ligands on)

IT CD3 (antigen)
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (TCR complex; T-cell response to interplay between costimulatory and pro-apoptotic signaling ligands for activation via)

IT T cell (lymphocyte)
 (activation; in response to interplay between costimulatory and pro-apoptotic signaling ligands)

IT T cell (lymphocyte)
 (memory; response to interplay between costimulatory and pro-apoptotic signaling ligands)

IT CD4-positive T cell
 (naive; response to interplay between costimulatory and pro-apoptotic signaling ligands)

IT T cell (lymphocyte)
 (proliferation; in response to interplay between costimulatory and pro-apoptotic signaling ligands)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:880214 HCAPLUS

DOCUMENT NUMBER: 136:133488

TITLE: Induction of antitumor immunity via intratumoral tetra-costimulator **protein transfer**

AUTHOR(S): **Zheng, Guoxing; Chen, Aoshuang;**
 Sterner, Raymond E.; Zhang, Paul J.; Pan, Tao;
 Kiyatkin, Nadya; **Tykocinski, Mark L.**

CORPORATE SOURCE: Department of Pathology and Laboratory Medicine,
 University of Pennsylvania, Philadelphia, PA, 19104,
 USA

SOURCE: Cancer Research (2001), 61(22), 8127-8134
 CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors' group recently described a novel two-step Fcγ1 fusion **protein transfer** method, which entails the docking of Fcγ1 fusion proteins onto cells precoated with chemical palmitated

protein A (pal-prot A). In the present study, the authors have adapted this **protein transfer** method, originally used in an ex vivo context, for in situ tumor cell engineering, and in so doing, the authors have evaluated its utility for the induction of antitumor immunity via combinatorial costimulator **protein transfer** on to tumor cell surfaces. The feasibility of "painting" cells with preformed conjugates of a murine B7-1 costimulator derivative, B7-1-Fcyl, and pal-prot A in a single step was first established ex vivo. Next, B7-1-Fcyl:pal-prot A transfer was accomplished in vivo by directly injecting the preformed conjugates into highly aggressive L5178Y-R lymphomas grown intradermally in syngeneic mice. The presence of cell surface-associated B7-1 epitopes on cells of the injected tumors was documented by flow cytometric anal. of cells recovered subsequently from the injected tumors. B7-1-Fcyl, along with Fcyl fusion protein derivs. of three addnl. costimulators (Fcyl-4-1BBL, CD48-Fcyl, and Fcyl-CD40L) geared toward a variety of immune effectors, were together preconjugated with pal-prot A and injected directly into tumor beds. Significantly, this "tetra-costimulator" combination, delivered intratumorally, induced complete tumor regression in .apprx.45% of treated mice, whereas control injections of pal-prot A alone had no therapeutic effect. Furthermore, there was evidence for systemic antitumor immunity in that tumor-specific CTLs were detected in spleens recovered from cured mice, and these mice were uniformly protected against tumor rechallenge at distant tumor sites. Hence, combinatorial costimulator transfer, coupled to intratumoral delivery, may have special advantages for the induction of antitumor immunity.

- CC 15-8 (Immunochemistry)
ST antitumor immunity T cell costimulator fusion protein
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(4-1BB, fusion products, with Fcyl; palmitoylated protein
A-mediated transfer to tumor membranes and induction of anti-tumor
response)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A, palmitoylated; transfer to tumor membranes of T-cell costimulatory
mol. fusion proteins is facilitated by)
IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD40-L (antigen CD40 ligand), fusion products, with Fcyl;
palmitoylated protein A-mediated transfer to tumor membranes and
induction of anti-tumor response)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD48 fusion products, with Fcyl; palmitoylated protein
A-mediated transfer to tumor membranes and induction of anti-tumor
response)
IT Lymphoma
(T-cell; costimulatory mol.-Fcyl fusion proteins, complexed with
palmitoylated protein A, are adsorbed to tumor membranes and elicit
anti-tumor response)
IT T cell (lymphocyte)
(cytotoxic; costimulatory mol.-Fcyl fusion proteins, complexed
with palmitoylated protein A, are adsorbed to tumor membranes and
elicit anti-tumor response by)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fragments, Fcyl, fusion products with costimulatory mols.;
palmitoylated protein A-mediated transfer to tumor membranes and

induction of anti-tumor response)

IT CD80 (antigen)
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (fusion products, with Fcγ1; palmitoylated protein A-mediated
 transfer to tumor membranes and induction of anti-tumor response)

IT Fusion proteins (chimeric proteins)
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (of T-cell costimulatory mols. with Fcγ1 are transferred to tumor
 cell membranes and elicit anti-tumor response)

IT Adsorption
 (of costimulatory mol.-Fcγ1 fusion proteins complexed with
 palmitoylated protein A to tumor membranes)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:507826 HCAPLUS

DOCUMENT NUMBER: 135:89545

TITLE: Methods for **protein transfer** using
 lipidated proteins and fusion proteins

INVENTOR(S): Tykocinski, Mark L.; Chen, Aoshuang
 ; Zheng, Guoxing

PATENT ASSIGNEE(S): TR Associates, L.L.C., USA

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049825	A1	20010712	WO 2001-US103	20010103
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6316256	B1	20011113	US 2000-476828	20000103
EP 1246901	A1	20021009	EP 2001-900311	20010103
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003519240	T2	20030617	JP 2001-550354	20010103
PRIORITY APPLN. INFO.:			US 2000-476828	A 20000103
			WO 2001-US103	W 20010103

AB Methods for transferring one or more proteins to a cell are disclosed. The protein or proteins to be transferred are in the form of a fusion protein, and contain at least one domain encoding for a protein or peptide having trans signaling and/or adhesion function. The fusion protein is transferred to a cell by binding to a lipidated protein, which has been incorporated into the cell membrane. Methods for using cells which have undergone **protein transfer** according to the present methods are also disclosed. This includes use in a cancer vaccine, use for treatment of cancer or autoimmune disease, and use in determining costimulator threshold levels. A B7-1-Fcγ1 fusion protein was transferred to K562 cells using palmitated protein A.

IC ICM C12N005-00
ICS C12N005-02; C12N005-06; C12N005-16

CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 6, 15, 63

ST **protein transfer** chimeric trans signaling cell
adhesion; lipidated **protein transfer** fusion protein;
palmitated protein A transfer CD80 fusion Fc IgG1

IT Antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(4-1BB ligand, fusion protein containing; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(A, lipidated; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)

IT Lipids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(C12-C22, protein lipidated with; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)

IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(CD40-L (antigen CD40 ligand), fusion protein containing; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)

IT CD antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(CD48, fusion protein containing; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)

IT Animal cell line
(CHO; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)

IT Animal cell line
(Daudi, EL-4; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(G, lipidated; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)

IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

- (ICAM-1 (intercellular adhesion mol. 1), fusion protein containing;
protein transfer methods using lipidated proteins and
fusion proteins having trans signaling or adhesion function)
- IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(ICAM-2 (intercellular adhesion mol. 2), fusion protein containing;
protein transfer methods using lipidated proteins and
fusion proteins having trans signaling or adhesion function)
- IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(ICAM-3 (intercellular adhesion mol. 3), fusion protein containing;
protein transfer methods using lipidated proteins and
fusion proteins having trans signaling or adhesion function)
- IT Immunoglobulin receptors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(IgG type I, fusion proteins with B7-1; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Animal cell line
(JURKAT, Fas-pos., apoptosis of; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Animal cell line
(JY; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Animal cell line
(K562; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Cell proliferation
(T cell; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Immunity
(alloimmunity; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Fas antigen
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(apoptosis of Jurkat cell pos. for; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Transplant and Transplantation
(autotransplant; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

- (coinhibitor, fusion protein containing; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT T cell (lymphocyte)
(costimulator activation thresholds determination in; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(costimulator, fusion protein containing; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Immunomodulators
(domain with function of; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT CD8 (antigen)
CD80 (antigen)
CD86 (antigen)
Fas ligand
LFA-3 (antigen)
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(fusion protein containing; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(heat-stable, fusion protein containing; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT CD30 (antigen)
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(ligand, fusion protein containing; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(lipidated; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(membrane, type I or II, fusion protein containing portion of; **protein transfer** methods using lipidated proteins and fusion proteins having trans signaling or adhesion function)
- IT Affinity
(of fusion protein for lipidated protein; **protein transfer** methods using lipidated proteins and fusion proteins

- having trans signaling or adhesion function)
- IT T cell (lymphocyte)
(proliferation; **protein transfer** methods using
lipidated proteins and fusion proteins having trans signaling or
adhesion function)
- IT Antitumor agents
Autoimmune disease
Cell
Cell adhesion
Cell membrane
Protein motifs
Signal transduction, biological
Temperature effects, biological
Therapy
(**protein transfer** methods using lipidated proteins
and fusion proteins having trans signaling or adhesion function)
- IT Fusion proteins (chimeric proteins)
Proteins, general, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
(**protein transfer** methods using lipidated proteins
and fusion proteins having trans signaling or adhesion function)
- IT Cytokines
Interleukin 2
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(**protein transfer** methods using lipidated proteins
and fusion proteins having trans signaling or adhesion function)
- IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study); PROC (Process)
(signal-transducing; **protein transfer** methods using
lipidated proteins and fusion proteins having trans signaling or
adhesion function)
- IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study); PROC (Process)
(single chain, Fv derivative, fusion protein containing; **protein
transfer** methods using lipidated proteins and fusion proteins
having trans signaling or adhesion function)
- IT Vaccines
(tumor; **protein transfer** methods using lipidated
proteins and fusion proteins having trans signaling or adhesion
function)
- IT Antitumor agents
(vaccines; **protein transfer** methods using lipidated
proteins and fusion proteins having trans signaling or adhesion
function)
- IT Apoptosis
(with Fc-hFasL fusion protein anchored with palmitated protein A;
protein transfer methods using lipidated proteins and
fusion proteins having trans signaling or adhesion function)
- IT Interferons
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(γ ; **protein transfer** methods using lipidated
proteins and fusion proteins having trans signaling or adhesion

function)
 IT 57-10-3DP, Palmitic acid, conjugates with protein A
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (protein transfer methods using lipidated proteins
 and fusion proteins having trans signaling or adhesion function)
 IT 14464-31-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (protein transfer methods using lipidated proteins
 and fusion proteins having trans signaling or adhesion function)
 REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:52445 HCAPLUS
 DOCUMENT NUMBER: 132:206675
 TITLE: Hierarchical costimulator thresholds for distinct
 immune responses: application of a novel two-step Fc
 fusion protein transfer method
 AUTHOR(S): Chen, Aoshuang; Zheng, Guoxing;
 Tykocinski, Mark L.
 CORPORATE SOURCE: Department of Pathology and Laboratory Medicine,
 University of Pennsylvania, Philadelphia, PA, 19104,
 USA
 SOURCE: Journal of Immunology (2000), 164(2), 705-711
 CODEN: JOIMA3; ISSN: 0022-1767
 PUBLISHER: American Association of Immunologists
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Activation of T cells is dependent upon coordinate engagement of Ag and
 costimulator receptors on their surfaces. In the case of the Ag receptors
 (TCRs), activation thresholds have been defined, with the number of TCRs that
 must be triggered to stimulate cytokine secretion by individual activated
 T cells differing for the various cytokines. In the present study, the
 authors have determined whether comparable activation thresholds exist for the
 costimulator receptors on T cells. To facilitate this type of quant.
 costimulator anal., the authors developed a novel two-step protein
 transfer approach that permits delivery of graded amts. of
 proteins to APC surfaces. By adding a human B7-1.Fcγ1 (Fc
 domain of human IgG1) fusion protein to cells precoated with palmitated
 protein A, fine titration of the B7-1 extracellular domain was achieved. The
 B7-1.Fcγ1 reincorporated into cell membranes by this method
 retained costimulator function, as measured by an in vitro proliferation
 assay. The degree of proliferation was dependent on the surface d. of
 B7-1.Fcγ1. Significantly, the threshold B7-
 1.Fcγ1 d. required for cytokine production differed between
 IFN-γ and IL-2 and mirrored the hierarchy (IFN-γ < IL-2)
 described previously for the TCR activation threshold. Hence, this study
 invokes a novel protein transfer strategy to establish
 that the levels of surface costimulator on APCs can dictate both the
 magnitude and the quality of evoked T cell responses. The notion of
 costimulator receptor activation thresholds emerges.
 CC 15-2 (Immunochemistry)
 ST B7 fusion protein cytokine T cell activation
 IT Proteins, specific or class
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (A, palmitoylated; for incorporation of B7-1 fusion protein into
 antigen-presenting cells)

IT Immunoglobulins
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (G1, Fc, fusion products, with B7-1; threshold dependence for induction of T-cell cytokine expression by)

IT CD80 (antigen)
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (fusion products, with IgG1 Fc; threshold dependence for induction of T-cell cytokine expression by)

IT Antigen-presenting cell
 Cell activation
 Immunological accessory cell
 T cell (lymphocyte)
 (threshold dependence for B7 fusion protein costimulatory induction of cytokine expression by T-cells)

IT Fusion proteins (chimeric proteins)
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (threshold dependence for B7 fusion protein costimulatory induction of cytokine expression by T-cells)

IT Interleukin 2
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (threshold dependence for B7 fusion protein costimulatory induction of cytokine expression by T-cells)

IT Interferons
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (γ; threshold dependence for B7 fusion protein costimulatory induction of cytokine expression by T-cells)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:732755 HCAPLUS

DOCUMENT NUMBER: 132:235617

TITLE: **Protein transfer of**
 glycosyl-phosphatidylinositol (GPI)-modified murine
 B7-1 and B7-2 costimulators

AUTHOR(S): Brunschwig, Elaine B.; Fayen, John D.; Medof, M.
 Edward; **Tykocinski, Mark L.**

CORPORATE SOURCE: Institute of Pathology, Case Western Reserve
 University, Cleveland, OH, 44106, USA

SOURCE: Journal of Immunotherapy (1999), 22(5), 390-400
 CODEN: JOIMF8; ISSN: 1053-8550

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The feasibility of using **protein transfer** as a means for enhancing the immunogenicity of murine tumor cells was evaluated. Glycosyl-phosphatidylinositol (GPI)-modified variants of the murine costimulators B7-1 (CD80) and B7-2 (CD86), designated B7-1•GPI and B7-2•GPI, resp., were immunoaffinity-purified from CHO-K1 cells transfected with glutamine synthetase amplification/expression constructs encoding each of these chimeric proteins. The proteins, once purified in detergent-depleted pseudomicelles, were exogenously incorporated into the membranes of several different murine tumor lines (EL-4, SMUCC-1, BW5147.3, P815, Ag104A, and EMT6). Successful membrane painting with the B7•GPI proteins was documented by immunofluorescence and flow

cytometry, and membrane integration was verified by demonstrating that the reincorporated proteins were phosphatidylinositol-phospholipase C-sensitive, glycosyl-phosphatidylinositol-phospholipase D-resistant, and refractory to removal with dimyristylphosphatidylcholine vesicles. Significantly, B7-1•GPI and B7-2•GPI could be together copainted onto EL-4 cell surfaces with no interference observed between the two. A standard in vitro proliferation assay was used to show that both of the B7•GPI proteins retained costimulator function after membrane reincorporation. These findings further validate the therapeutic potential of **protein-transferred** costimulator•GPIs and pave the way for their combinatorial use in animal tumor models.

CC 15-2 (Immunochemistry)

Section cross-reference(s): 3

ST glycosylphosphatidylinositol modified tumor cell **protein transfer**

IT CD80 (antigen)

CD86 (antigen)

RL: BAC (Biological activity or effector, except adverse); BPN

(Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)

(-GPI; **protein transfer** of glycosyl-

phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators)

IT Animal cell line

(Ag104A; **protein transfer** of glycosyl-

phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators and incorporation into)

IT Animal cell line

(Bw5147.3; **protein transfer** of glycosyl-

phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators and incorporation into)

IT Animal cell line

(EL4; **protein transfer** of glycosyl-

phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators and incorporation into)

IT Animal cell line

(EMT6; **protein transfer** of glycosyl-

phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators and incorporation into)

IT Animal cell line

(P-815; **protein transfer** of glycosyl-

phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators and incorporation into)

IT Animal cell line

(Smucc-1; **protein transfer** of glycosyl-

phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators and incorporation into)

IT Glycophospholipids

RL: BAC (Biological activity or effector, except adverse); BPN

(Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)

(phosphatidylinositol-containing; **protein transfer** of

glycosyl-phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators)

IT Cell proliferation

(**protein transfer** of glycosyl-phosphatidylinositol

(GPI)-modified murine B7-1 and B7-2 costimulators)

IT Antigens

RL: BAC (Biological activity or effector, except adverse); BPN

- (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**protein transfer** of glycosyl-phosphatidylinositol
(GPI)-modified murine B7-1 and B7-2 costimulators and enhancement as)
- IT Cell membrane
(**protein transfer** of glycosyl-phosphatidylinositol
(GPI)-modified murine B7-1 and B7-2 costimulators and incorporation
into tumor)
- IT Fusion proteins (chimeric proteins)
RL: BAC (Biological activity or effector, except adverse); BPN
(Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**protein transfer** of glycosyl-phosphatidylinositol
(GPI)-modified murine B7-1 and B7-2 costimulators as)
- IT Transformation, genetic
(**protein transfer** of glycosyl-phosphatidylinositol
(GPI)-modified murine B7-1 and B7-2 costimulators instead of)
- IT Immunotherapy
(**protein transfer** of glycosyl-phosphatidylinositol
(GPI)-modified murine B7-1 and B7-2 costimulators use in)
- IT Genetic methods
Protein engineering
(**protein transfer** or protein painting;
protein transfer of glycosyl-phosphatidylinositol
(GPI)-modified murine B7-1 and B7-2 costimulators)
- IT Vaccines
(tumor; **protein transfer** of glycosyl-
phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators
as)
- IT Antitumor agents
(vaccines; **protein transfer** of glycosyl-
phosphatidylinositol (GPI)-modified murine B7-1 and B7-2 costimulators
as)

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:16595 HCAPLUS

DOCUMENT NUMBER: 130:236039

TITLE: Engineering cellular cancer vaccines: gene and
protein transfer options

AUTHOR(S): Tykocinski, Mark L.

CORPORATE SOURCE: Department of Pathology and Laboratory Medicine,
University of Pennsylvania, Philadelphia, PA, 19104,
USA

SOURCE: Gene Therapy of Cancer (1999), 301-318. Editor(s):
Lattime, Edmund C.; Gerson, Stanton L. Academic: San
Diego, Calif.
CODEN: 67DQAI

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review with 174 refs. discussing the two major classes of cellular
cancer vaccines, dendritic and tumor cell vaccines, both of which are
designed to activate tumor-specific CD8-pos. cytotoxic T-cell effectors.
The focus here is on the cellular engineering tools that are currently
available for the ex vivo production of both classes of cancer vaccines,
especially
those tools applicable to engineering cell surfaces. Most studies to date

have concentrated upon ex vivo gene transfer approaches, but openness to other cellular engineering strategies is needed.

CC 15-0 (Immunochemistry)

ST review genetic engineering cancer vaccine; **protein transfer** cancer vaccine review

IT Cell membrane
(cancer vaccine development using costimulatory mol. transfer to tumor cell membrane)

IT Neoplasm
(genetic engineering and **protein transfer** modification of tumor cells for vaccines against)

IT Cytokines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(genetic engineering of cytokine expression by tumor cells for cancer vaccines)

IT CD80 (antigen)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(genetic engineering of immune costimulatory mol. expression by tumor cells for cancer vaccines)

IT Dendritic cell
(in genetic engineering and **protein transfer** modification of tumor cells for cancer vaccines)

IT Genetic engineering
(of tumor cells for cancer vaccines)

IT CD86 (antigen)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(transfer to tumor cell membrane in relation to cancer vaccine development)

IT Antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-associated; in genetic engineering and **protein transfer** modification of tumor cells for cancer vaccines)

IT Vaccines
(tumor; genetic engineering and **protein transfer** modification of tumor cells for)

IT Antitumor agents
(vaccines; genetic engineering and **protein transfer** modification of tumor cells for)

REFERENCE COUNT: 174 THERE ARE 174 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L18 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:357220 HCAPLUS

DOCUMENT NUMBER: 125:31912

TITLE: Methods for engineering antigen-presenting cells

INVENTOR(S): Tykocinski, Mark L.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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 WO 9612009 A2 19960425 WO 1995-US12718 19951011
 WO 9612009 A3 19961010

W: CA, JP

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.:

US 1994-324125

19941014

AB A **protein transfer** method for producing a cell having a defined MHC: nominal antigen peptide or costimulator on its membrane. The method comprises (1) first contacting the external portion of the cells with an externally applied artificial lipid-modified MHC polypeptide able to bind a nominal antigen peptide, and (2) second contacting the cells with the nominal antigen peptide so that the artificial lipid-modified MHC polypeptide binds the antigen peptide. Demonstrated in examples were production of glycosylphosphatidylinositol-modified human class I MHC, purification of HLA-A2.1:GPI/β2m heterodimers, cytolytic T lymphocyte recognition of C1R cells coated with HLA-A2.1:GPI/β2m heterodimer and HLA-A2.1-restricted peptide complexes, preparation of veto cell by **protein transfer** of an HLA-A2.1:GPT/β2m peptide complex, treatment of chronic active hepatitis patient with hepatitis B virus-specific T cells amplified using HLA-A2.1:GPI:hepatitis B virus peptide-coated dendritic cells, and a functional artificial GPI-modified costimulator (B7-1:GPI).

IC ICM C12N005-08

CC 15-1 (Immunochemistry)

ST antigen presenting cell glycosylphosphatidylinositol modified MHC

IT Antigens
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (B7-3, costimulator peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)

IT Animal cell line
 (C1R; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)

IT Fibronectins
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (costimulator peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)

IT Immunological accessory cell
 Membrane, biological
 (engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)

IT Peptides, biological studies
 RL: BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)

IT Lipids, uses
 RL: MOA (Modifier or additive use); USES (Uses)
 (engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)

IT Animal cell
 (lipid-modified MHC:nominal antigen peptide-containing; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)

IT Gene
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (transfer; engineering of antigen-presenting cells by contacting with

- lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Antigens
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(B 7.2, costimulator peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Lymphocyte
(B-cell, activated; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Antigens
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(B7/BB-1, costimulator peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Antigens
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD58, costimulator peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-A2.1, engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Glycoproteins, specific or class
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-1 (intercellular adhesion mol. 1), costimulator peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Glycoproteins, specific or class
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-2 (intercellular adhesion mol. 2), costimulator peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility antigen complex), class I, engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility antigen complex), class II, engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex), engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Lymphocyte
(T-cell, antigen-specific; engineering of antigen-presenting cells by

- contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Sialoglycoproteins
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VCAM-1 (vascular cell adhesion mol. 1), costimulator peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chimeric, engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Leukocyte
(dendritic cell, engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Virus, animal
(hepatitis B, peptide; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Glycophospholipids
RL: MOA (Modifier or additive use); USES (Uses)
(phosphatidylinositol-containing, engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT Antigens
RL: BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor-associated, engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT 26062-48-6, Polyhistidine
RL: MOA (Modifier or additive use); USES (Uses)
(as tag; engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)
- IT 9013-20-1, Streptavidin
RL: MOA (Modifier or additive use); USES (Uses)
(engineering of antigen-presenting cells by contacting with lipid-modified MHC polypeptide and nominal antigen peptide)

L18 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:983881 HCAPLUS
DOCUMENT NUMBER: 124:27559
TITLE: Glycosylphosphatidylinositol-modified murine B7-1 and B7-2 retain costimulator function
AUTHOR(S): Brunschwig, Elaine B.; Levine, Elie; Trefzer, Uwe; Tykocinski, Mark L.
CORPORATE SOURCE: Inst. Pathol., Case Western Res. Univ., Cleveland, OH, 44106, USA
SOURCE: Journal of Immunology (1995), 155(12), 5498-505
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glycosylphosphatidylinositol (GPI)-modified variants of murine B7-1 and B7-2 cell surface costimulators were produced via chimerization with alternative GPI-modification signal sequences from decay-accelerating factor (DAF). GPI anchorage was verified by demonstrating phosphatidylinositol-specific phospholipase C (PI-PLC) sensitivity of the chimeric polypeptides in both immunofluorescence/flow-cytometric and immunopptn. analyses. The various GPI-modified chimeric B7-1:DAF and B7-2:DAF polypeptides were shown to retain costimulator function, in both

an in vitro proliferation assay and an in vivo triggering of cytotoxicity assay. The findings indicate that costimulator function for both B7-1 and B7-2 is not dependent upon native hydrophobic transmembrane anchorage. Moreover, the functionality of the GPI-modified variants in enhancing the immunogenicity of the murine T lymphoma line EL-4 suggests a novel route for generating APC-centered immunotherapeutics, including cellular cancer vaccines, that is based upon **protein transfer** of GPI-modified costimulators.

CC 15-2 (Immunochemistry)
 ST Glycosylphosphatidylinositol modified murine antigen B7
 IT Antigens
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (B 7.2, glycosylphosphatidylinositol-modified murine B7-1 and B7-2 retain costimulator function)
 IT Antigens
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (B7/BB-1, glycosylphosphatidylinositol-modified murine B7-1 and B7-2 retain costimulator function)
 IT Glycophospholipids
 RL: MOA (Modifier or additive use); USES (Uses)
 (phosphatidylinositol-containing, decay-accelerating factor-derived; glycosylphosphatidylinositol-modified murine B7-1 and B7-2 retain costimulator function)

L18 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:698694 HCAPLUS

DOCUMENT NUMBER: 121:298694

TITLE: **Protein transfer** of preformed MHC-peptide complexes sensitizes target cells to T cell cytotoxicity

AUTHOR(S): Huang, Jui-Han; Getty, Robert R.; Chisari, Francis V.; Fowler, Patricia; Greenspan, Neil S.; **Tykocinski, Mark L.**

CORPORATE SOURCE: Inst. Pathol., Case Western Res. Univ., Cleveland, OH, 44106, USA

SOURCE: Immunity (1994), 1(7), 607-13
 CODEN: IUNIEH; ISSN: 1074-7613

PUBLISHER: Cell Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recombinant GPI-anchored HLA-A2.1 (HLA-A2.1-GPI/ β 2m) was used as a **protein transfer** vehicle to deliver a hepatitis B virus antigenic peptide to the surfaces of cytotoxic T cell targets. Empty HLA-A2.1-GPI/ β 2m was first produced in *D. melanogaster* contrasfectants and immunoaffinity purified. Cell coating with HLA-A2.1-GPI/ β 2m effectively presented a hepatitis B virus peptide to peptide-specific HLA-A2.1-restricted T cell clones in cytotoxicity assays. **Protein transfer** of functional GPI-modified class I MHC-antigenic peptide complexes represents a novel strategy for delivering functional antigenic complexes to cell surfaces that bypasses limitations of gene transfer and permits control of antigenic peptide densities at cell surfaces.

CC 15-2 (Immunochemistry)

ST **protein transfer** MHC peptide complex; cytotoxic T cell antigen complex transfer

IT *Drosophila melanogaster*

Transformation, genetic

(in recombinant glycosylphosphatidylinositol-anchored protein complexes

- preparation in *Drosophila melanogaster*)
- IT Cytolysis
(recombinant glycosylphosphatidylinositol-anchored **protein transfer** of preformed MHC-peptide complexes sensitizes target cells to T cell cytolysis)
- IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-A2.1, complexes; recombinant glycosylphosphatidylinositol-anchored **protein transfer** of preformed MHC-peptide complexes sensitizes target cells to T cell cytolysis)
- IT Lymphocyte
(T-cell, cytotoxic, recombinant glycosylphosphatidylinositol-anchored **protein transfer** of preformed MHC-peptide complexes sensitizes target cells to T cell cytolysis)
- IT Glycophospholipids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(phosphatidylinositol-containing, HLA-A2.1 complexes; recombinant glycosylphosphatidylinositol-anchored **protein transfer** of preformed MHC-peptide complexes sensitizes target cells to T cell cytolysis)